UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

IN RE BIOPURE SECURITIES LITIGATION	)	**CIVIL ACTION NO. 03-12628-NG**

DEFENDANTS' REPLY MEMORANDUM OF LAW IN SUPPORT OF THEIR MOTION TO DISMISS THE CONSOLIDATED AMENDED CLASS ACTION COMPLAINT

BIOPURE CORPORATION, THOMAS A. MOORE, CARL W. RAUSCH, HOWARD P. RICHMAN, CHARLES A. SANDERS, RONALD F. RICHARDS and J. RICHARD CROUT,

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Defendants Biopure Corporation ("Biopure" or the "Company"), Thomas A. Moore, Carl W. Rauch, Howard P. Richman, Charles A. Sanders, Ronald F. Richards and J. Richard Crout (collectively, the "Defendants" or Messrs. Moore, Rausch, Richman, Sanders, Richards and Crout as the "Individual Defendants"), respectfully submit this reply to Plaintiffs' Opposition to their Motion to Dismiss ("Opposition" or "Opp.").

Preliminary Statement

The Opposition rests entirely on Plaintiffs' misguided belief that Defendants were required to disclose the FDA's clinical hold on a proposed, uninitiated and undisclosed clinical trial for early-stage data-gathering in support of a *new indication* for Hemopure -- *trauma* patients. Plaintiffs believe that the FDA's safety concerns regarding a proposed test for this distinct indication for Hemopure somehow meant that Hemopure was deemed unsafe much more broadly and with regard to Biopure's publicly disclosed biologics license application ("BLA") for marketing approval of Hemopure in *orthopedic surgery*. The BLA had been submitted to the FDA after *completion* of all three phases of clinical trials, which *met primary safety and efficacy endpoints*, and after Hemopure received regulatory *approval* in South Africa while continuing trials for various uses (including trauma) in Europe and South Africa. *See* Defendants' Memorandum of Law in Support of Their Motion to Dismiss ("Defs. Brief") at 3-4, 7. Arising from that erroneous belief, Plaintiffs contend that virtually all of Biopure's public statements during the purported class period were somehow false and misleading because Biopure did not disclose the clinical hold of the proposed new indication for Hemopure in trauma patients. Plaintiffs are seriously mistaken.

As a matter of FDA regulatory procedure, FDA's safety concerns regarding Biopure's new and separate indication for trauma are not automatically ascribable to Hemopure generally or in the indication of orthopedic surgery submitted in Biopure's BLA. Separate indications for a biologic are reviewed and treated separately, and FDA safety concerns for one indication do not, unless FDA says otherwise, apply to other indications. The Opposition thus rests on a mistaken assertion about the FDA review process, presuming that FDA action regarding one

indication of a drug or biologic is *ipso facto* imputed to another indication for the same drug or biologic. Plaintiffs fail to cite to a single factual allegation of the Amended Complaint (because they cannot) asserting that the FDA clinical hold in trauma was imputed to Hemopure's regulatory progression via the BLA in orthopedic surgery. In short, the Opposition (and with it the Amended Complaint) rests on an "apples and oranges" theory that cannot as a matter of law predicate 10b-5 claims.

Even if disclosure were required regarding the FDA clinical hold on an undisclosed, uninitiated, proposed indication, which FDA itself treated separately from the BLA, the Opposition fails to rehabilitate the Amended Complaint's fatal deficiencies with respect to pleading the required strong inference of scienter. In effect, Plaintiffs predicate scienter on the SEC's issuance of Wells Notices and the fact (standing alone) that one of the Individual Defendants traded Biopure stock. Tellingly, the Opposition fails to cite any case where mere reference to an SEC investigation was held sufficient to allege scienter, likely because there are none. Indeed, such a pleading practice cannot withstand Rule 11. Nor does the Opposition cite to any case where allegations of stock trades alone -- without requisite allegations of circumstances that could raise suspicion -- were deemed sufficient. The Plaintiffs have not met their burden of proof as to any of the Individual Defendants. Accordingly, the Amended Complaint should be dismissed with prejudice.

REPLY

I. THE OPPOSITION IS ERRONEOUSLY PREDICATED ON THE MISTAKEN ASSUMPTION THAT BIOPURE HAD A DUTY TO DISCLOSE THE FDA'S CLINICAL HOLD ON THE NEW, UNINITIATED AND SEPARATE TRAUMA INDICATION FOR HEMOPURE.

The Opposition launches Plaintiffs' argument with an assertion that the clinical hold in trauma "caused the FDA to halt further human clinical trials and delay the approval process, and cast serious doubt on the likelihood of obtaining FDA approval." Opp. at 2. *Nothing* in the Amended Complaint, however, alleges facts to show that the clinical hold on trauma "halted" *the BLA approval process*, nor could Plaintiffs so allege. As noted, the proposed possible trauma

trial (which was only in the infancy stage of a proposed protocol, a written outline for a clinical trial) was separate and distinct from the BLA, and accordingly, received separate FDA treatment. Defs. Brief at 9. Without allegations making the connection that Plaintiffs imply in their brief, Plaintiffs' extensive arguments that virtually all of Biopure's disclosures regarding the BLA were rendered misleading by the absence of disclosure of the clinical hold are superfluous. Accordingly, the Amended Complaint, resting entirely on a theory that the clinical hold and safety concerns in trauma should have been disclosed, must be dismissed.

A. The Opposition Fails To Identify Allegations That Connect The BLA And Proposed Trauma Trial To Support A Nondisclosure Claim.

As explained in Defendants' opening brief, FDA review and approval is indication-specific. The FDA approval process involves a series of steps, including clinical trials and culminating in the submission of a BLA for each indication. The FDA's review logically focuses on efficacy and safety *with respect to the indication proposed*. Obviously, a biologic deemed sufficiently safe for one form of treatment may be deemed too risky in another. Accordingly, when clinical trials (*i.e.*, data gathering for an intended BLA) are proposed to the FDA, the agency's primary objective is to judge whether evidence shows that the biologic is sufficiently safe *with respect to that proposed indication* to permit the trials to proceed. Defs. Brief at 5-6.

FDA regulations spell this critical point out. In 21 C.F.R. § 312.42, "Clinical holds and requests for modification," FDA is required to apply clinical holds to the indication ("IND") at issue, and FDA must specify which investigations are subject to clinical hold:

> (a) General. A clinical hold is an order issued by FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. *The clinical hold order may apply to one or more of the investigations covered by an IND.* When a proposed study is placed on clinical hold, subjects may not be given the investigational drug. When an ongoing study is placed on clinical hold, no new subjects may be recruited to the study and placed on the investigational drug; patients already in the study should be taken off therapy involving the investigational drug unless specifically permitted by FDA in the interest of patient safety.
>
> (d) Imposition of clinical hold. The clinical hold order may be made by telephone or other means of rapid communication or in writing. *The clinical hold*

> *order will identify the studies under the IND to which the hold applies, and will briefly explain the basis for the action. . . .*

21 C.F.R 312.42 (emphasis added).

Indeed, numerous drugs and biologics are rejected by the FDA for particular indications based on safety concerns, later to be approved in other indications. Perhaps the most well-known example is Thalidomide, a sedative approved in Europe in the sixties that ultimately caused severe birth defects when taken during pregnancy. The Thalidomide tragedy was actually the impetus for much of the regulatory testing protocols in place with FDA today. See *Giving Thalidomide a Second Chance*, Herbert Burkholz (member of FDA's public affairs staff) FDA Consumer Magazine (September-October 1997) (attached as Exhibit 1 to Defendants' Appendix of Documents, hereafter "App.").[1] Yet in the 1990's, the FDA began permitting clinical trials for new IND's for Thalidomide, (*id.*) and in 1998 the drug was actually approved for use in treating lesions resulting from leprosy. *See* FDA's Thalidomide Approval Letter, App. Exh. 2. The FDA's discussion of the history of Thalidomide and its approval is instructive on the point. *See* Supervisory Review of NDA 20-785, Janet Woodcock, MD, July 7, 1998 , App. Exh. 3.

Accordingly, the FDA's clinical hold on a new proposed indication for Hemopure in trauma patients due to "safety concerns" did not mean the FDA harbored the same concerns for use of Hemopure in orthopedic surgery, the indication at issue in Biopure's publicly disclosed BLA. Importantly, the FDA here *required* Biopure to submit its trauma protocol under an IND separate from Biopure's orthopedic surgery indication, the subject of the BLA. *See* Defs. Brief.

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[1] Plaintiffs take issue with Defendants' reliance on articles concerning the FDA on this 12(b)(6) motion, contending that Defendants have offered facts outside the Amended Complaint. Opp. at 23, n.12. Plaintiffs are mistaken, as the materials submitted in support of Defendants' Motion to Dismiss are either referenced in the Amended Complaint, are central to Plaintiffs' claims or are public documents, the authenticity of which is not in dispute and of which this Court may accordingly take judicial notice of at this juncture. *E.g., Lynch v. Board of State Examiners of Electricians*, 218 F. Supp. 2d 3, 7 n.7 (D. Mass. 2002) ("courts have made narrow exceptions for documents the authenticity of which are not disputed by the parties; for official public records; for documents central to plaintiffs' claim; or for documents sufficiently referred to in the complaint").

at 10.[2] Aside from Plaintiffs' conclusory assertions that Defendants were on "notice" about problems with the orthopedic surgery BLA due to the clinical hold in trauma, (*e.g.*, Am. Compl. ¶ 31), the Amended Complaint is *devoid* of any allegations of fact to that effect -- there are no allegations that the FDA placed any trials in orthopedic indications on clinical hold, there are no allegations pleading that the FDA communicated to Biopure safety concerns regarding the BLA, and there are no factual allegations pleading that the BLA's approval was derailed by the clinical hold in trauma. Indeed, the closest Plaintiffs come to drawing any link between the clinical hold in trauma and Biopure's orthopedic surgery BLA is their allegation that the FDA's safety concerns for the trauma indication arose from data submitted as part of the BLA. *E.g.*, Opp. at 25-26. If FDA had safety concerns for Hemopure in orthopedic surgery, however, it presumably would have communicated as much, and Plaintiffs would have alleged the same. Yet the Amended Complaint contains no such allegation.

On the contrary, *after* notifying Biopure of the clinical hold on the proposed trauma trial, FDA wrote the Company about the BLA and stated *only* that FDA was taking an additional 90 days to review the BLA, due to the submission of new data by the Company. *See* May 30, 2003 Press Release, App. Exh. 4 at 1.

In short, Plaintiffs' repeated assertions that the FDA's safety concerns in trauma were material to Biopure's orthopedic surgery BLA are both factually unsupported and legally contradicted by FDA's clinical hold regulations and procedure.

B. The Opposition Fails To Identify A Basis For Imposing A Duty To Disclose The Trauma Clinical Hold.

Plaintiffs acknowledge that 10b-5 liability based on an omission first requires a duty to disclose the alleged omitted information and claim they have asserted facts forming the basis of

[2] Plaintiffs' arguments that the FDA's safety concerns in its initial review of the trauma protocol cast "serious doubt" on the likely approval of the BLA for the orthopedic surgery indication are conclusory and entirely unsupported. (Opp. at 23, 26; A.C. 31). Similarly, Plaintiffs' argument that the FDA decided to suspend review of the BLA due to safety concerns fails to identify -- as it must -- any fact to that effect. (Opp. at 25).

such a duty. Opp. at 21-23. Plaintiffs then offer three assertions in support of their theory that Biopure had a duty to disclose the clinical hold placed on its proposed new indication for trauma, each of which is patently without merit.

First, Plaintiffs assert that Defendants did not disclose safety concerns "about Hemopure" or the clinical hold "cast[ing] serious doubt on the likelihood of approval." Opp. at 22-23. Wholly apart from the absence of any allegation of fact to show that the FDA's safety concerns were not limited to the proposed trauma trial but rather involved Hemopure vis-à-vis the BLA, the assertion merely begs the question. Nondisclosure in and of itself can hardly be deemed a basis for imposing a duty to disclose.

Second, Plaintiffs argue that Biopure never disclosed the "true reason for the delay" in the FDA's review of the BLA, citing to paragraphs 62, 67, 77, 82, 85 and 88 of the Amended Complaint. Opp. at 23. Curiously, there is no allegation in any of those paragraphs (or anywhere else in the Amended Complaint) to show what the "true reason" for the delay might have been. Plaintiffs' argument is without basis in the Amended Complaint. (The reason stated by FDA and the Company's press release was that FDA needed additional time to review data submitted by the Company as an amendment to the BLA.) *See* App. Exh. 4 at 1.

Third, Plaintiffs contend that Defendants disclosed (after receiving Wells Notices) that the delay in the review process for the BLA resulted from safety concerns regarding the trauma protocol citing paragraphs 32 and 33 of the Amended Complaint. Opp. at 23. No such allegation appears in those paragraphs. Rather, paragraph 33 merely quotes Biopure's December 24 press release, stating that the company's amendment to the BLA resulted in a three-month delay. A.C. ¶33. Again, Plaintiffs' argument is without basis in the Amended Complaint.

C. Plaintiffs Cite No Case Requiring The Disclosure Of FDA Communications Concerning An Uninitiated, Proposed Clinical Trial For An Indication Separate From The Company's Disclosed FDA-Submitted Indications.

Precisely because the FDA's clinical hold was issued only with respect to an undisclosed, uninitiated proposed clinical trial for a new indication, and not with respect to the BLA, the cases cited by Plaintiffs in support of their assertion that Defendants had a duty do disclose are

inapposite. (Opp. at 23-24). *Cf. In re Sepracor, Inc. Sec. Litig.*, 308 F. Supp.2d 20 (D. Mass. 2004) (court found that omission of adverse side effects was material where trial had been *initiated*); *In re PLC Systems, Inc. Sec. Litig.*, *In re PLC Systems, Inc. Sec. Litig*., 41 F. Supp. 2d 106 (D. Mass. 1999) (plaintiffs sufficiently alleged that defendants misrepresented clinical effectiveness and regulatory progress of its *initiated* medical device-clinical studies); *In re Cell Pathways, Inc. Sec. Litig.*, 2003 U.S. Dist. Lexis 8584 (E.D. Penn. 2003) (defendants misrepresented progress and results of its *initiated* Phase III clinical trial); *In re Neopharm, Inc. Sec. Litig.*, 2003 U.S. Dist. Lexis 1862 (N.D. Ill. 2003) (defendants misrepresented facts about *initiated* Phase II clinical trials); *In re Biogen Sec. Litig.*, 179 F.R.D. 25 (D. Mass. 1997) (defendants made statements claiming positive results of clinical trials but failed to disclose FDA's concerns about shortcomings of trials); *In re British Biotech*, Release No. 41505, 1999 SEC Lexis 1162 (defendants made statements claiming that their clinical trials demonstrated efficacy but failed to disclose FDA's contrary opinion). Unlike these cases, Plaintiffs here have not alleged false or misleading statements about the results of an *initiated, publicly disclosed* clinical study (creating the need to update prior disclosures).

Plaintiffs' reliance on *In re Transkaryotic Therapies, Inc. Sec. Litig.*, 319 F. Supp. 2d 152, 159-60 (D. Mass. 2004) (Opp. at 26-27) is also mistaken. In *Transkaryotic*, the court held that the defendant's failure to disclose FDA's reasons for denying approval of defendant's drug (clinical studies were methodologically flawed, did not show efficacy and in order to generate acceptable data, company would have to start over from scratch) was actionable. Notably, the defendant in *Transkaryotic* ensured the public that approval of its product was a "when not if proposition," despite the fact that the FDA informed it that its product did not show efficacy. *Id.* at 160. Thus, the court held that the defendant should have disclosed the FDA's findings as to efficacy so as to make defendant's optimistic statements not misleading. *Id. Transkaryotic* is far removed from the facts alleged in this case where the alleged "bad news" did not concern the

BLA, did not allegedly indicate that the entire methodology was flawed, and Defendants did not guarantee the ultimate approval of its product.[3]

Plaintiffs also claim that Defendants' reliance upon *In re MedImmune, Inc. Sec. Litig.*, 873 F. Supp. 953 (D. Md. 1995) is misplaced since Defendants here purportedly failed to disclose FDA concerns which "cast doubt upon obtaining approval of a BLA." (Opp. at 27-29; Defs. Br. at 13-15). As noted, Plaintiffs' claim that the FDA concerns "cast doubt on obtaining approval of the BLA" is without basis in the Amended Complaint, and Plaintiffs cannot again amend their complaint via the Opposition.

Plaintiffs also contend that *In re Biogen* is inapposite because, unlike the defendants there, Biopure here "failed to disclose 'the most relevant and disappointing aspect' about the Hemopure BLA, which was that the FDA had [i] suspended its review and [ii] asked for additional information from Biopure and [iii] had placed a hold on the proposed Trauma Trial due to the FDA's Safety Concerns . . . ." Opp. at 29 (enumeration added). With regard to (i) and (ii), *Plaintiffs in fact allege that Biopure did disclose that the FDA had suspended its review and asked for additional information*. *E.g.*, A.C.¶ 66. The Opposition therefore simply mischaracterizes the Amended Complaint. As for (iii), again, that Biopure did not disclose the trauma trial did not somehow create a duty to disclose the information. *See In re Biogen*, 179 F.R.D. at 37 (dismissing challenges to defendant's statement where there was no duty to disclose the FDA's reservations and concerns about the efficacy of defendant's drug and stating that as a general proposition, defendants "have no duty to report their ongoing discussions with the FDA during the review process").[4]

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[3] To the contrary, Biopure repeatedly and accurately disclosed the risks associated with obtaining FDA approval of Hemopure. (*See* Defs. Brief at 7-9, 18).

[4] In addressing plaintiffs' claim that the defendant failed to disclose that its clinical trials failed to reach pre-defined secondary endpoints, the court noted that the "most relevant and disappointing aspect" of the clinical trial results (failure to reach the primary endpoint) already entered the marketplace. *In re Biogen*, 179 F.R.D. at 39. Contrary to Plaintiffs' representations (Opp. at 28), the court did not state this as the reason for rejecting plaintiffs' claims that defendant was required to disclose the FDA reservations (or "status of obtaining FDA approval") (Opp. at 28).

Finally, Plaintiffs' attempt to distinguish *Chu v. Sabratek*, 100 F. Supp. 2d 827 (N.D. Ill. 2000), on the ground that, in *Chu*, "the company's regulatory difficulties with the FDA were known to the public" (Opp. at 29), is unavailing. While the *Chu* court did make such an observation in passing, the point was not argued by the defendants, and so the Court went on to analyze the duty to disclose independent of the public knowledge of FDA problems the company experienced. Plaintiffs here are silent on that dispositive holding in *Chu*: "[s]imply receiving a number of letters from the FDA listing regulatory shortcomings does not portend ultimate FDA denial of the recipient's application." *Chu*, 100 F. Supp. 2d 827, 834-35.

II. THE OPPOSITION FAILS TO IDENTIFY ANY BASIS FOR ASSERTING THAT DEFENDANTS' STATEMENTS CONCERNING THE STATUS OF THE *ORTHOPEDIC SURGERY BLA* WERE EITHER FALSE OR MISLEADING.

Defendants' statements during the purported class period, made in the context of Biopure's publicly disclosed efforts toward FDA approval of the BLA for orthopedic surgery, were neither false nor misleading, and the Opposition fails to raise any colorable issue to the contrary.[5] In their opening brief, Defendants explained in detail (based on the text of the statements themselves) the factual accuracy of historical statements and the non-actionable character of others as mere corporate optimism or as bespeaking caution. (*See* Defs. Brief at 19-32, detailing why each alleged false and misleading statement is non-actionable). In response, Plaintiffs argue at length that these statements -- all concerning Biopure and its prospects in light of its BLA for its core indication in orthopedic surgery -- were somehow false or misleading because Defendants did not disclose the clinical hold on its non-public, uninitiated new indication for Hemopure in the trauma setting.[6] Again, the Opposition's arguments stem from

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[5] Since the statements are true, Plaintiffs' claim that Defendants Moore and Richards falsely certified that Biopure's SEC filings did not contain any misleading statements or omission (Opp. at 41) is unsupported. In addition, Plaintiffs do not challenge the lack of a *single* allegation in the Amended Complaint that attributes a false or misleading statement to Defendants Crout, Sanders or Rausch. Both the PSLRA and Rule 9(b) require Plaintiffs to "distinguish among those they sue and enlighten *each* defendant as to his or her part in the alleged fraud." *Coates*, 26 F. Supp. 2d at 914 (emphasis added).

[6] Plaintiffs rely on *In re Transkaryotic* in support of the argument that Defendants' statements disclosing the risks of not obtaining FDA approval were false and misleading. (*See* Opp. at 31-32).

(footnote continued on next page)

Plaintiffs' fundamental misconceptions of the FDA review process, based on a mistaken belief that the FDA's review of Hemopure in one indication is wholly transferable to another. As shown above, Plaintiffs' contentions are mistaken.[7]

As Plaintiffs have offered nothing by way of facts that purportedly should have been disclosed regarding the Hemopure BLA, the only matter warranting attention on reply is the sole statement challenged by Plaintiffs that did bear on Biopure's intentions to pursue a trauma program.[8] In particular, Plaintiffs argue that Biopure falsely and misleadingly stated in March 2003 that "completion of the pivotal RESUS clinical trial of Hemopure in trauma is contingent upon further funding . . . ." Opp. at 35 (citing A.C. ¶49). The "RESUS clinical trial of Hemopure in trauma" referenced by the Company involved a collaborative trial that would be pursued by the Navy along with Biopure. A.C. ¶49. While the RESUS trial would involve trauma once funding was secured, Plaintiffs point to no allegation of fact that the trials were the

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Transkaryotic is distinguishable, however, since the defendant there misrepresented present facts in its disclaimers concerning the risks of failure to obtain FDA approval of its drug, which review process had been publicly disclosed. *See In re Transkaryotic*, 319 F. Supp. 2d at 161, n.10 (statement that FDA might "request additional information" was materially misleading since the FDA had already requested additional clinical trials due to its criticisms of the efficacy of defendant's trials -- "such language is materially different from the fact that the FDA, had, in essence, already made that request"). Unlike the defendants in *Transkaryotic*, Defendants here did not make any disclaimers that contradicted statements or directives by the FDA. Furthermore, Defendants did not "guarantee" that the FDA would approve its product.

[7] In any event, "[t]he mere fact that an investor might find information interesting or desirable is not sufficient to satisfy the materiality requirement." *Lucia v. Prospect Street High Income*, 36 F.3d 170, 175 (1st Cir. 1994). A statement is not misleading merely because there is an undisclosed fact bearing "some relation to the subject matter" of the statement. *In re Boston Tech. Sec. Litig.*, 8 F. Supp. 2d 43 (D. Mass. 1998) (dismissing challenges to statement where there was no duty to disclose allegedly omitted information). Given that Hemopure had been approved for use in South Africa, used to conclusion in 22 clinical trials, had met its primary safety and efficacy endpoints, and the clinical hold made no statement about the likely outcome of the ongoing Hemopure BLA review or the overall safety of the product, information about the clinical hold may have been of interest to a reasonable investor, but not material.

[8] Defendants rely on their Memorandum of Law In Support of their Motion to Dismiss with respect to the factual accuracy or non-actionable character of the challenged statements. As Plaintiffs' Opposition rests primarily on mistaken assertions about the purported need to disclose the trauma clinical hold and safety concerns in that indication, Defendants' arguments need not be repeated here.

same indication or protocol (including for instance the same dosing, patient population, availability of blood, etc.) as the new indication for trauma that became the subject of the FDA's clinical hold. Again, Plaintiffs cannot impute the significance of the FDA clinical hold in trauma in the hospital setting to the contemplated RESUS trials conducted in conjunction with the military. In addition, this statement is itself forward looking and speculative as it talks merely about a funding contingency, another variable in connection with initiating a possible future trial.

III. DEFENDANTS' FORWARD-LOOKING STATEMENTS ARE NON-ACTIONABLE AND THE OPPOSITION FAILS TO SHOW OTHERWISE.

A. Defendants' Statements Concerning the Status of the BLA and Anticipated Revenue From Marketing Hemopure are Forward-Looking and Thus Non-Actionable under the PSLRA.

Plaintiffs argue that Defendants' statements concerning the status of the BLA and anticipated marketing revenue are unprotected by the safe harbor provisions of the PSLRA as a result of the nondisclosure of the clinical hold which, according to Plaintiffs, "bore directly on the future of both the Hemopure BLA and the Company." (Opp. at 44; A.C. at ¶¶ 45, 50, 53, 58, 63 and 72). According to Plaintiffs, their challenge is based on the non-disclosure of alleged "present facts," and therefore the safe harbor protection is inapplicable. Opp. at 43.

Again, Plaintiffs persistently disregard the distinction between the FDA's clinical hold of the uninitiated and undisclosed proposed trauma trial and the Hemopure orthopedic surgery BLA which review was ongoing. Thus, Plaintiffs' contention that the FDA's safety concerns about the undisclosed proposed trauma trial somehow rendered misleading Defendants' forward-looking statements concerning Biopure made in the context of its disclosed BLA, miss the mark. (Opp. at 42; *see also* Defs. Brief at 17-19, discussing immateriality of clinical hold).[9]

[9] Indeed, the only forward-looking statement challenged in the Amended Complaint and addressed in the Opposition that did bear on trauma was outside the purported class period and, in any event, clearly not actionable. In January of 2003, Biopure reported that it "has identified trauma as its next clinical development priority and is working with a committee of independent civilian and military trauma experts to broaden its trauma program." A.C. ¶ 26. The statement plainly indicates nothing more than an intent to pursue trauma indications in the future, and Plaintiffs have alleged nothing to show that Defendants did not so intend.

B. Defendants' Forward-Looking Statements are Protected by the Safe Harbor Provisions of the PSLRA.

Plaintiffs also contend that Defendants' forward-looking statements do not qualify for safe harbor protection because they were accompanied by unmeaningful, boilerplate cautionary language in light of the "known risks" arising from the FDA's safety concerns in the newly proposed trauma indication.[10] (Opp. at 45). The PSLRA's safe harbor provision protects forward-looking statements that are either: accompanied by meaningful cautionary statements, immaterial, or not pled as having been made "with actual knowledge…that the statement was false and misleading." 15 U.S.C. § 78u-5(c)(1)(A)(i)-(B). The challenged forward-looking statements are non-actionable under all three prongs. (*See* Defs. Brief at 20, 23-32).

Importantly, Biopure's cautionary language was far from boilerplate, and Plaintiffs' Opposition on this point is unavailing. Notably, Plaintiffs fail even to cite to Biopure's purportedly "boilerplate" risk disclosures, let alone attempt to explain how the detailed disclosures were "boilerplate." Opp. at 45-47. Plaintiffs' bald assertions in their brief cannot be reconciled with Biopure's cautionary language:

> *If We Fail to Obtain FDA Approval We Cannot Market Hemopure in the United States*
>
> We will not be able to market Hemopure in the United States until we receive FDA approval. We have filed an application for approval with the FDA, and the application was accepted for review on October 1, 2002. We believe that our completed pivotal Phase III clinical trials are consistent with the FDA's most recent guidance on the design and efficacy and safety endpoints required for approval of products such as Hemopure for use in surgical indications. **However, the FDA could change its view, require a change in study design or require additional data or even further clinical trials, including trials for indications other than those for which the pending application seeks approval, prior to approval of Hemopure.** The FDA could refuse to grant a marketing authorization. Trials are expensive and time-consuming. Obtaining FDA

[10] Plaintiffs claim that a failed class action case against Biopure, *Meyer v. Biopure*, 221 F. Supp. 2d 195 (D. Mass. 2002), put Defendants on notice that failure to disclose the FDA's safety concerns was both material and misleading, since the Judge in that case "made clear that omissions regarding the safety of Hemopure would have been actionable." (Opp. at 48). Plaintiffs' reasoning is flawed. *Meyer* does not support Plaintiffs' claims since the FDA's clinical hold and safety concerns concerning the proposed trauma trial categorically did *not* mean that Hemopure was "unsafe." (*See* Defs. Brief at 35).

> approval generally takes years and consumes substantial capital resources with no assurance of ultimate success.

See Form S-3 dated April 11, 2003, April 16, 2003, June 19, 2003, July 2, 2003 and August 22, 2003 (App. Exhs. 5-9, respectively) (emphasis added).[11]

Here, the very risk complained of by Plaintiffs was specifically disclosed, unlike a "vague or blanket disclaimer" merely warning the reader that the investment had risks. *See In re Donald Trump Casino Sec. Litig.*, 7 F.3d 357, 371 (3d Cir. 1993). To the contrary, it was "substantive and tailored to the specific predictions made in the allegedly misleading statement." *Viropharma Inc. Sec. Litig.*, 2003 U.S. Dist. Lexis 5263 at *27 (E.D. Penn. 2003) (citing *In re Donald Trump Casino*, 7 F.3d at 371-372.

Further, for the same reasons explained below and in Defendants' opening brief, Plaintiffs have also utterly failed to plead facts which could establish "actual knowledge" as required to render the Company's forward-looking statements actionable.

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[11] Similarly, the January and April 2003 Form 10-Qs, warned investors in part that: "[E]xcept for strictly historical information contained herein, matters discussed in this report constitute forward-looking statements. There can be no assurance that Biopure will be able to commercially develop Hemopure, that necessary regulatory approvals will be obtained, that anticipated milestones will be met in the expected timetable, that any clinical regulatory approvals will be obtained, that any clinical trials will be successful, or that any approved product will attain market acceptance and be manufactured and sold in the quantities anticipated. Actual results may differ from those projected in forward-looking statements due to risks and uncertainties that exist in the Company's operations and business environment."

The registration statements contained detailed risk factors with the following headings: (1)"If We Fail to Obtain FDA Approval, We Cannot Market Hemopure in the United States"; (2) "If We Fail to Obtain Regulatory Approvals in Foreign Jurisdictions, We Will Not Be Able to Market Hemopure Abroad"; (3) "*We Cannot Expand Indications for Our Products Unless We Receive Approval For Each Proposed Indication*"; (4) "If We Cannot Find Appropriate Marketing Partners, We May Not Be Able to Market and Distribute Hemopure Effectively"; (5) "If we Cannot Generate Adequate, Profitable Sales of Hemopure, We Will Not Be Successful"; (6) "If We Cannot Obtain Market Acceptance of Hemopure, We Will Not Be Able to Generate Adequate, Profitable Sales." (*See* App. Exhs. 5-9) (emphasis added).

IV. THE COMPLAINT MUST BE DISMISSED BECAUSE PLAINTIFFS HAVE UTTERLY FAILED TO ALLEGE SUFFICIENT FACTS SUPPORTING A STRONG INFERENCE OF SCIENTER AS TO EACH DEFENDANT.

A. Scienter May Not Be Inferred From an SEC Staff Recommendation of Investigation.

Rather than plead with particularity specific facts giving rise to each defendant's requisite level of scienter, Plaintiffs attempt to rely on the issuance of the Wells Notices to validate their claim that Defendants had the requisite intent to defraud the public. They argue that under the standard for a motion to dismiss, they are entitled to reasonable inferences of scienter based on the SEC's Wells Notices issued to certain of Defendants. Plaintiffs cite no case for that novel proposition, likely because there is none.

If the Wells Notices could be used, standing alone, to establish Defendants' scienter, the PSLRA's pleading requirements would be meaningless. In effect, every time the SEC initiates an investigation, whether it concludes in withdrawal of the investigation, consent decree (which typically neither admits nor denies liability), or otherwise, securities plaintiffs could pass the PSLRA's high hurdle. Further, under Rule 11, the Wells Notices cannot be relied upon by Plaintiffs to establish scienter. *See Geinko v. Padda*, 2002 WL 276236 at *5 (N.D. Ill. 2002) ("The pervasive defect in the Amended Complaint…is that it does not make clear what Plaintiffs directly allege as fact, and what Plaintiffs merely are asserting that someone else has alleged. In other words…*Plaintiffs cannot shirk their Rule 11 obligation to conduct an appropriate investigation into the facts that is reasonable under the circumstances by merely stating that 'the SEC alleges' certain additional facts*") (emphasis added).

Nonetheless, claiming that SEC is Plaintiffs' "confidential source," the Opposition posits that the First Circuit's decision in *In re Cabletron Systems, Inc.*, 311 F.3d 11 (1st Cir. 2002) regarding the ability of securities plaintiffs to rely on "confidential sources" in satisfying the PSLRA are "*a fortiori* applicable" to this case. (Opp. at 53-54). The First Circuit in *Cabletron* held that plaintiffs are not required to name anonymous sources at the pleading stage to satisfy the PSLRA's particularity requirements as long as they "plead with particularity sufficient facts to support [their] beliefs [concerning the false and misleading statements]." *Cabletron*, 311 F.3d

at 30, citing *Novak v. Kasaks*, 216 F.3d 300, 313 (2d Cir. 2000).

Plaintiffs' attempt to extend *Cabletron* to the instant context fails both as a matter of logic and analogy. Notably, the plaintiffs in *Cabletron* relied on statements from a confidential source to provide "specific descriptions of the precise means through which the [alleged] fraud occurred." *Cabletron*, 311 F.3d at 30. Here, Plaintiffs seek to draw an inference of scienter from the mere fact that the SEC staff recommended civil proceedings against certain of Defendants -- not from facts provided by the Wells Notices themselves. In any event, like Plaintiffs, the SEC still has the burden of proving that Defendants acted with scienter with respect to 10b-5 claims. *See Aaron v. SEC*, 446 U.S. 680, 701-02 (1980).[12] Thus, Plaintiffs cannot rely on the Wells Notices to prove the requisite scienter for each defendant. [13]

Plaintiffs also cite to *In re Health Management, Inc. Sec. Litig.*, 970 F. Supp. 192 (E.D.N.Y. 1997) and *In re Hamilton Bankcorp. Sec. Litig.*, 194 F. Supp. 2d 1353 (S.D. Fla. 2002) in support of their scienter argument. (Opp. at 55). These, too, are inapposite and fail to support Plaintiffs' arguments. Plaintiffs in *Health Management* specifically pled numerous facts establishing a strong inference of scienter, one of which was notice of the SEC's "informal inquiry" into the defendant's actions. 970 F. Supp. at 204.[14] Additional facts pled with

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[12] Importantly, in often relied upon civil injunctive proceedings under Sections 17(a)(2) and 17(a)(3), unlike securities plaintiffs, the SEC may prevail by merely establishing negligence and not scienter. *Id.*

[13] Plaintiffs also rely on *Adams v. Kinder-Morgan, Inc.*, 340 F.3d 1083, 1102-03 (10th Cir. 2003) and *In Re Phillip Servs. Corp. Inc.*, 2004 U.S. Dist. Lexis 9261 (S.D.N.Y. 2004) to support their contention that inferences of Defendants' scienter may be drawn from the Wells Notices. (Opp. at 54). The reasoning in these cases, however, involves pleading fraud with particularity and do not specifically focus on scienter. *See e.g., Adams*, 340 F.3d at 1102-03 (lists factors to be evaluated in determining whether securities fraud claim made on information and belief satisfies particularity requirement of PSLRA); *In Re Phillip Servs*., 2004 U.S. Dist. Lexis 9261 at 44-45 (addressing defendants' argument that because plaintiffs' complaint relied exclusively on information and belief, plaintiffs' failure to name certain relevant witnesses they interviewed in preparing complaint was additional ground for dismissal).

[14] There are countless securities and related cases *dismissing* complaints for failure to state a claim that, as is the case here, were filed following the initiation of an SEC investigation. *E.g., In re Interbank Funding Corp. Sec. Litig*, 329 F. Supp. 2d 84 (D.D.C. 2004); *In re Syncor Intern. Corp. Sec. Litig*, 327 F. Supp. 2d 1149 (C.D. Cal. 2004); *In re Nash Finch Co. Sec. Litig.*, 323 F. Supp. 2d 956 (D.

(footnote continued on next page)

particularity included, however: (1) a senior manager's presence at a meeting at which the alleged inventory fraud was developed, (2) the senior manager approval of the plan and instruction that it be put into effect; and (3) letters from outside auditors alerting the senior manager of problems with accounts receivable. *Id*. Unlike the *Health Management* plaintiffs, Plaintiffs here have failed to plead *any* facts suggesting an inference of scienter, let alone the strong inference required by the PSLRA.

Similarly, the *Hamilton* plaintiffs alleged in part that one of the defendants had violated generally accepted accounting principles (GAAP). *In re Hamilton*, 194 F. Supp. 2d at 1359. The court found that plaintiffs pled that defendant "knew and recklessly disregarded, or was severely reckless in not knowing of, a number of red flags which would have exposed the purported fraud" including a government banking agency's investigation of the defendant's alleged accounting improprieties, which resulted in adverse findings. *Id.* at 1359. Unlike *Hamilton*, the SEC investigation here did not begin prior to the time the Defendants made the allegedly false and misleading statements to serve as a "red flag."

B. Plaintiffs Fail To Even Address The Reasons Stated In Defendants' Brief As To Why Their Alleged "Additional Facts" Do Not Raise Any Inference, Let Alone The Requisite Strong Inference, Of Scienter.

In Defendants' opening brief, Defendants explained the deficiencies in Plaintiffs' allegations of other purported facts that are alleged to give rise to an inference of scienter.[15]

(footnote continued from previous page)

Minn. 2004); *In re Corrpro Sec. Litig.*, 2003 WL 23138459 (N.D. Oh. 2003); *In re Keyspan Corp. Sec. Litig.*, 2003 WL 1702279 (E.D.N.Y. 2003); *Geinko v. Padda*, 2002 WL 276236 (N.D. Ill. 2002); In *re Envoy Corp. Sec. Litig.*, 133 F. Supp. 2d 647 (M.D. Tenn. 2001).

[15] *See* Defs. Brief. at 34-37 (decision in *Meyer v. Biopure*, 221 F. Supp. 2d 195 (D. Mass. 2002) not a basis for scienter as FDA's clinical hold of the proposed trauma trial did *not* indicate that Hemopure was unsafe; changes to Biopure's risk disclosures after the SEC began its investigation do not show scienter because changes were made prior to Defendants having any notice or knowledge of the SEC's investigation; Defendant Moore's statement with respect to competitor's product Hemosol being on clinical hold distinguishable because that company announced that a trial had begun and was ongoing then had to announce when it was halted due adverse effects; success of Hemopure as critical to Company insufficient because bare motives to raise capital and ensure corporate success could be imputed to every publicly-owned enterprise).

Plaintiffs fail to address these points, and instead simply repeat the allegations in the Amended Complaint. Opp. at 59, 63-64.[16]

C. Defendants' Allegations Of Insider Trading Do Not Add To Their Purported Bases For Raising the Required Strong Inference Of Scienter.

In their opposition, Plaintiffs acknowledge the point made by Defendants that *only* allegations of "*unusual* trading or trading at *suspicious* times or in suspicious amounts" may support an inference of scienter. Opp. at 66 (quoting *Greebel*, 194 F.3d at 197). Plaintiffs then argue, incredulously, that there was "massive insider trading." (Opp. at 65), sweeping under the rug the fact that there are *no* allegations of *any* trading by Messrs. Crout, Moore, Richards, Richman or Sanders -- *five* of the six Individual Defendants. That circumstance alone tends to negate an inference of scienter. *See e.g., In Re PEC Solutions Sec. Litig.*, No. 03-CV-331 2004 WL 1854202 *15 (E.D. Va. May 25, 2004) (fact that only one of the individual defendants engaged in trading tended to negate scienter).

More to the point, however, allegations of insider trading only may present support for an inference of scienter when the trading is alleged to be *suspicious*, based on particularized facts concerning the context and history of trading. *See e.g., Carney v. Cambridge Tech. Partners, Inc.*, 135 F. Supp. 2d 235, 256 (D. Mass. 2001); *Greebel v. FTP Software Inc*., 194 F.3d 185, 198 (1st Cir. 1999) (defendants' trading must be "unusual" and "well-beyond [their] normal patterns of trading"). As the First Circuit held in *Greebel*, "mere pleading of insider trading, without regard to either context or the strength of the inferences to be drawn, is not enough." 194 F.3d at 198. As Judge Young has held, "[o]ne fact necessary to a showing of unusualness is the amount

[16] The only efforts Plaintiffs make beyond repeating the allegations of the Amended Complaint are at pages 56-59, wherein Plaintiffs contend that, due to their positions at Biopure, the importance of Hemopure's approval to the Company, alleged interactions with the FDA and "controls" at the Company to keep abreast of material events, Defendants "must have" known of the clinical hold and safety concerns in the proposed trauma protocol. These allegations might arguably provide an inference that the Defendants would have some knowledge of material events concerning the BLA -- the Company's core indication to which it had allegedly devoted nearly all its attention for years. The same cannot be reasonably inferred, however, with regard to a single proposed clinical trial in a distinct and separate indication in the early-stage data gathering phases.

of trading that the insider conducted before or after the class period." *In re Peritus Software Services, Inc. Sec. Litig.*, 52 F. Supp. 2d 211, 224 (D. Mass. 1999). In *Peritus*, as in this case, "the Class has alleged only that insider trading occurred, not that it was unusual or suspicious," requiring dismissal. *Id.* Indeed, the only facts alleged by Plaintiffs are Defendant Rausch's and Biopure's sales and amounts through July and August of 2003, ending *four months before* the "bad news" was disclosed in December, 2003. Judge Woodlock deemed insider sales in similar amounts insufficient to support an inference of scienter in *In re Focus Enhancements, Inc. Sec. Litig.*, 309 F. Supp. 2d 134 (D. Mass. 2001), because, as here, "the timing of the insider trading does not appear very suspicious. The sales did not occur before a big 'event' unknown to the public." *Id.* at 164.

Plaintiffs cite *In re PerkinElmer, Inc. Sec. Litig.*, 2003 U.S. Dist. Lexis 17506 at *24-25 (D. Mass. 2003), noting that there, a complaint was sustained where defendants sold "substantial blocks of stock during the period." (Opp. at 66). *PerkinElmer*, however, actually illustrates the deficiencies of the Amended Complaint here. In that case, the plaintiffs also alleged that there had been *no record of similar sales* in the prior three years and that *the sales were not part of a pattern of usual trading*. *Id.* at 24. Here, Plaintiffs have not alleged any irregularity in Biopure and Rausch's selling in terms of timing or pattern. (Opp. at 65-67; A.C. at ¶¶ 94-104, 114). Indeed, aside from the allegations of amounts sold and retained during the class period, the Amended Complaint is devoid of the particularized allegations of circumstances raising suspicion that are required to credit insider trading allegations toward an inference of scienter.

Plaintiffs' allegations of insider trading are mere surplusage, providing no support for any inference of scienter.

CONCLUSION

For the foregoing reasons and for the reasons stated in Defendants' Memorandum in Support of their Motion to Dismiss, Defendants respectfully request that this Court dismiss Plaintiffs' Consolidated Amended Complaint in its entirety.

Respectfully submitted,

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Dated: January 24, 2005

CERTIFICATE OF SERVICE

I hereby certify that a true copy of the above pleading was electronically served upon the attorneys of record for all parties on January 24, 2005.

Raquel J. Webster